**The First Step Towards Treating Cone Photoreceptor Degeneration?**

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Review of “[Daylight Vision Repair by Cell Transplantation](http://www.ncbi.nlm.nih.gov/pubmed/25183393)” from *Stem Cells* by Stuart P. Atkinson

Healthy functional cone photoreceptors mediate color vision and high visual acuity under light conditions and disorders which lead to their dysfunction currently have no restorative treatments [1, 2]. Cell based therapies are a potentially interesting strategy, although very little is known about cone photoreceptor transplantation [3]. To remedy this, the group of [Marius Ader](http://www.crt-dresden.de/research/crtd-core-groups/ader.html) ([CRTD/DFG-Center for Regenerative Therapies Dresden, Germany](http://www.crt-dresden.de/)) have taken advantage of a mouse model in which the neural retina leucine zipper (Nrl‐/‐) transcription factor is deficient, leading to the generation of mice with rod‐depleted retinas, instead containing only cone and cone‐like photoreceptors [4]. They now report on their studies of cone photoreceptor replacement in Stem Cells [5].

Adult Nrl‐/‐ mice expressed only cone-specific genes (PNA, s‐opsin and cone arrestin) in photoreceptors, and did not express rod‐specific genes (Nrl or rhodopsin), confirming the sole presence of cone/cone-like photoreceptors. The group then purified these cone photoreceptors from the mouse retina based on the CD73 cell surface antigen at several different stages of postnatal development in order to identify the optimal cell population. CD73-purification generated a relatively pure fraction of cells which expressed photoreceptor‐specific genes (Crx and S‐opsin), and transplantation of postnatal day 4 cells into wild type mouse retina mediated optimal integration into the outer nuclear layer (ONL) generating morphologically mature photoreceptors. The attached figure shows integrated cone–like photoreceptors two weeks following transplantation into the adult retina of wild‐type mice.

The authors also demonstrated that these cells integrated into retinas characterized by cone photoreceptor degeneration (Cpfl1 mutant mouse), displaying similar characteristics to cells formed after transplantation into the wild type mice. Interestingly, a much higher number of donor cells integrated into the Nrl-/- mouse retina, which resembles the pure cone photoreceptor environment in the human fovea. Assessment of donor cone‐like photoreceptor survival in wild type and Cpfl1 mice demonstrated that while cells survived to 6 months, the last time point assessed, the overall number of these cells reduced significantly with time.

Functionality was finally assessed through the recording of light‐mediated spiking activity of individual retinal ganglion cells (RGCs) by micro‐electrode arrays. While both wild type and Cpfl1 mice responded to low and medium light stimuli, Cpfl1 mice did not respond to high light intensities, thus displaying impaired cone photoreceptor function. However, after transplantation with cone‐like photoreceptors, Cpfl1 mice did respond to high light intensity – an encouraging finding.

This represents the first step towards a restoring daylight vision to those affected by debilitating disease such as age‐related macular degeneration (AMD), cone‐rod dystrophies, or late-stage retinitis pigmentosa (RP). The authors hope to further assess the cellular connectivity and cell-to-cell communication abilities of the donor cells, and to develop efficient differentiation techniques to derive cone cells from stem cells; in doing so taking us one step closer towards the clinical application of such an approach.

**References**

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